IN THE UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF TEXAS
HOUSTON DIVISION

LISA GAYLE BUTLER and DAVID A. HOLLAND, Individually and as Personal Representatives of the ESTATE OF MATY GAYLE HOLLAND, DECEASED,	§	No. 4:18-cv-898
Plaintiffs,	§	
v.	§	
JUNO THERAPEUTICS, INC.,	§	
Defendant.	§	JURY TRIAL DEMANDED

PLAINTIFFS' FIRST AMENDED COMPLAINT

Plaintiffs, Lisa Gayle Butler and David A. Holland, Individually and as Personal Representatives of the Estate of Maty Gayle Holland, Deceased, file this Original Complaint against Defendant, Juno Therapeutics, Inc., seeking damages for the wrongful death of their daughter, Maty Gayle Holland ("Maty"). Plaintiffs would respectfully show the Court as follows:

PRELIMINARY STATEMENT

1. Juno Therapeutics, Inc. ("Juno") is a development stage biopharmaceutical company that was founded in 2013. It is a wholly owned subsidiary of Celgene Corporation, one of the world's largest biotech companies. Celgene Corporation acquired Juno in March, 2018 based on a share valuation of $9 billion. Juno focuses on investigational cellular immunotherapies to treat various types of cancer, by genetically engineering a modification of a patient's own T cells, which are a type of white blood cell, which after modification can then recognize, target, and attack cancer cells. Juno has sought to test the efficacy and safety of its product candidates in clinical trials it sponsors (or otherwise supports or collaborates) through

various medical institutions. Juno's "most advanced clinical candidates,"[1] were JCAR014,[2] JCAR015, and JCAR017 ("CD19 Product Candidates"), that use a chimeric antigen receptor ("CAR") to empower the resulting "CAR-T" cells to treat various cancers, including a type of blood cancer known as acute lymphoblastic leukemia ("ALL"), by targeting the CD19 protein found on the surface of malignant B white blood cells.

2. Juno has not obtained the approval of the United States Food and Drug Administration ("FDA") for any of its products. To date, none of Juno's three CD19 Product Candidates has made it out of a Phase II clinical trial. Juno's CD19 Product Candidates are only investigational at this stage of their development and are not FDA approved prescription drugs.

3. Juno and its CAR-T competitors, most notably Novartis AG and Kite Pharmaceuticals, have been in an intense race to enroll participants in clinical trials and, ultimately, obtain FDA approval to market their immunotherapy drugs, which, once in the market, will be extraordinarily lucrative.[3] In the face of this competition, Juno's strategy was to (i) employ what it termed a "fast to market strategy" for JCAR015, (ii) designate its Phase II trial for JCAR015 as the "ROCKET Trial," and (iii) represent in its 2015 Annual Report that it was working towards "accelerated U.S. regulatory approval…as early as 2017," despite the fact that the Phase I trial for JCAR015, which Juno knew had dire safety concerns, was originally

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[1] Juno Therapeutics, Inc., SEC Form 10-K for the year ending Dec. 31, 2015, issued Feb. 29, 2016 ("2015 Annual Report"), at 4.

[2] Although Juno does not plan to move JCAR014 into registration trials, it is sufficiently similar to the other CD19 Product Candidates that Juno has reported it is using the JCAR014 clinical trial data to provide "insights on how to improve our efficacy and safety in patients . . . *across our portfolio*." *Id.* at 3-4 (emphasis added).

[3] Novartis's CAR-T treatment, Kymria, was the first CAR-T cell therapy to receive FDA approval and will reportedly cost $475,000 for a course of treatment. *See* https://www.statnews.com/2017/08/30/novartis-car-t-cancer-approved. Subsequently, Kite recently obtained FDA approval for its CAR-T treatment, Axi-Cel, which will reportedly cost $373,000 for a course of treatment. *See* https://www.fiercepharma.com/regulatory/kite-and-gilead-join-novartis-red-hot-car-t-market-early-axi-cel-approval.

represented by Juno not to be completed until 2017.[4]

4. Indeed, Juno was acutely aware of the direct relationship between its ability to enroll patients in clinical trials and its ability to obtain FDA approval for its products, as its 2015 Annual Report, issued on February 29, 2016, informs its investors and the investing public that "[i]f we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected."[5]

5. Among the reasons Juno identified for potential difficulties in enrolling patients in clinical trials were (i) "*treatment-related side effects* could . . . *affect patient recruitment* or the ability of enrolled subjects to complete the trial, or could result in potential product liability claims. . . . these occurrences may materially and adversely harm our business, financial condition and prospects," (ii) "*clinicians' and patients' perceptions* as to the potential advantages *and side effects* of the product candidate being studied in relation to other available therapies, including any new drugs or treatments that may be approved for the indications we are investigating," and (iii) "our clinical trials will compete *with other clinical trials* for product candidates that are in the same therapeutic areas as our product candidates, and *this competition will reduce the number and types of patients available to us*, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by *one of*

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[4] https://clinicaltrials.gov/ct2/show/NCT01044069; *In re Juno Therapeutics, Inc.*, No. 2:16-cv-01069-RSM, Dkt. No. 81, Defendants' Answer to Consolidated Amended Class Action Complaint for Violation of Federal Securities Laws (W.D. Wash. July 21, 2017) ("Juno Securities Lawsuit Answer") ¶¶ 3-4, 29; 2015 Annual Report, at 4-5.

[5] 2015 Annual Report, at 73.

our competitors."[6]

6. And Juno had ample cause for concern about the side effects of its drugs because, as discussed below, Juno knew that its CD19 Product Candidates have a documented history of life-threatening and fatal side effects. In fact, buried in its single-spaced, 304 page 2015 Annual Report, Juno admits that the "use of our product candidates could be associated with side effects or adverse events which can vary in severity from minor reactions to *death* and in frequency from infrequent to prevalent. . . .We have seen severe neurotoxicity or [severe cytokine release syndrome], in some cases leading to *death*, in a number of patients . . . using each of JCAR015, JCAR017, and JCAR014."[7]

7. Facing stiff competition from Novartis and Kite to enroll patients in its clinical trials, Juno's "fast to market strategy" led it to sacrifice patients' safety by advancing JCAR015 to a Phase II study 17 months early and by omitting, withholding, concealing, understating and misrepresenting known risks and side effects of its CD19 Product Candidates, primarily including severe cytokine release syndrome, severe neurotoxicity and death, including their severity and prevalence. The FDA never approved JCAR015 and Juno has recently decided to terminate any further testing of this investigational drug. Unfortunately, it is too late for Maty, who was given an infusion of JCAR015 in June 2016, after enrolling in Juno's ROCKET Trial, and died shortly thereafter.

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[6] *Id*. (emphasis added). Juno's 2014 and 2016 Annual Reports also expressed the same concerns regarding difficulties enrolling patients in its clinical trials due to clinicians' and patients' perceptions about safety and patients choosing to enroll in the clinical trials of Juno's competitors. *See* Juno Therapeutics, Inc., SEC Form 10-K for the year ending Dec. 31, 2014, issued March 18, 2015 ("2014 Annual Report"), at 63; Juno Therapeutics, Inc., SEC Form 10-K for the year ending Dec. 31, 2016, issued March 1, 2017 ("2016 Annual Report"), at 62. Here, Plaintiffs primarily rely upon the 2015 Annual Report because it reflects Juno's knowledge as of February 29, 2016, which is approximately three months before Maty signed her Informed Consent for the JCAR015 clinical trial in May 2016.

[7] *Id*. at 72 (emphasis added).

PARTIES

8. Plaintiff, Lisa Butler, is a citizen of the State of Texas and a duly appointed and qualified personal representative of the Estate of Maty Gayle Holland, Deceased. Ms. Butler was Maty's mother.

9. Plaintiff, David Holland, is a citizen of the State of Texas and a duly appointed and qualified personal representative of the Estate of Maty Gayle Holland, Deceased. Mr. Holland was Maty's father.

10. Defendant, Juno Therapeutics, Inc., is a Delaware corporation with its principal place of business in Seattle, Washington. It can be served with process by serving its registered agent, Corporation Service Company, 251 Little Falls Drive, Wilmington, Delaware 19808.

JURISDICTION AND VENUE

11. This Court has subject matter jurisdiction over this suit pursuant to 28 U.S.C. § 1332 because the amount in controversy exceeds the sum or value of $75,000 and the action is between citizens of the State of Texas on the one hand, and a citizen of the States of Delaware and Washington on the other hand.

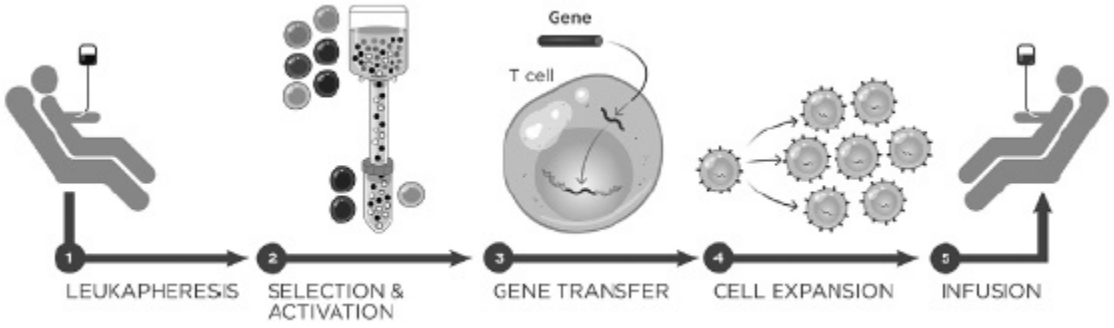
12. This Court has personal jurisdiction over Juno pursuant to TEX. CIV. PRAC. & REM. CODE § 17.042, because Plaintiffs' claims arise out of Juno's contacts with the State of Texas such that the exercise of such jurisdiction is consistent with due process under the United States Constitution. The ROCKET Trial was conducted at, among other sites, M.D. Anderson Cancer Center in Houston, Texas ("M.D. Anderson"), where Maty died.

13. Venue is proper in this judicial district pursuant to 28 U.S.C. § 1391(b)(2) because a substantial part of the events, acts, errors, omissions, and misrepresentations that give rise to the claims at issue in this case occurred in Houston, Harris County, Texas.

FACTUAL BACKGROUND

I. Juno's CAR-T Cell Therapy Treatment Process[8]

14. Juno's CAR-T immunotherapy uses a multi-step process, in which T cells are altered outside the body to recognize specific proteins on the surface of cancer cells so that those cancer cells can be destroyed, that Juno visually depicts as follows:



15. First, a patient's white blood cells are harvested in a process called leukapheresis. Next, with the white blood cells outside of the body, the T cells of interest are selected and activated. Third, gene sequences for the CAR construct are transferred into the T cell DNA using a viral vector, such as a lentivirus or a gamma retrovirus.[9] Fourth, the number of cells is expanded until the desired dose is reached.

16. Meanwhile, prior to the final step in the process, patients are given a pre-conditioning regimen of chemotherapy that is intended to deplete the patient's existing T-cells so that the genetically engineered T-cells can proliferate inside the patient's body. Until July 2016, Juno would administer the chemotherapy drug cyclophosphamide ("cy") to some patients, while some patients received a combination of both cy and another chemotherapy drug, fludarabine

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[8] Juno Securities Lawsuit Answer, ¶ 27; 2015 Annual Report, at 9.

[9] JCAR015 uses a gamma retrovirus, while JCAR014 and JCAR017 use a lentivirus. 2015 Annual Report, at 14.

("flu"). After reporting three patient deaths in July 2016, which included Maty, Juno discontinued the use of the flu-cy combination.

17. Finally, the genetically engineered T cells are infused back into the patient with the intention that they will recognize and kill cancer cells.

II. The FDA Drug Approval Process

18. Pursuant to FDA regulations, clinical trials for new drugs are conducted in three phases.

19. Phase I studies "are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness." 21 C.F.R. § 312.21.

20. Phase II studies are "typically well controlled" studies "conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug." *Id.*

21. Phase III studies are expanded studies "performed after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling. Phase 3 studies usually include from several hundred to several thousand subjects." *Id.*

22. A sponsor, such as Juno, is the entity that takes responsibility for and initiates a clinical trial by submitting to the FDA an Investigational New Drug Application ("IND"). 21 C.F.R. § 312.3. Once a sponsor has sufficiently conducted well-controlled multi-phase clinical trials, through its investigators, that demonstrate substantial evidence of efficacy and safety

consistent with the Food, Drug and Cosmetic Act of 1938, only then can the sponsor file a New Drug Application ("NDA") with the FDA seeking approval to market the drug in a specific dose for the treatment of a specific condition or "indication." The NDA must also specify how the drug will be manufactured, packaged, and labeled. The FDA can only grant approval if objective scientific evidence establishes that the requisite statutory criteria have been satisfied.

23. "Sponsors are responsible for selecting qualified investigators, providing them with the information they need to conduct an investigation properly, ensuring proper monitoring of the investigations, ensuring that the investigations [are] conducted in accordance with the general investigational plan and protocols contained in the IND, maintaining an effective IND with respect to the investigations, and ensuring that FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug." 21 C.F.R. § 312.50.

24. Before the clinical trial begins, a sponsor is required to give each participating clinical investigator an investigator brochure, which is a comprehensive document summarizing the body of known information about an investigational product, including, *inter alia*, "pharmacological and toxicological effects of the drug in animals and, to the extent known, in humans," "a summary of information relating to safety and effectiveness in humans obtained from prior clinical studies," and "a description of possible risks and side effects to be anticipated on the basis of prior experience with the drug under investigation or with related drugs, and of precautions or special monitoring to be done as part of the investigational use of the drug." 21 C.F.R. §§ 312.25(a)(5), 312.55.

25. "The sponsor shall, as the overall investigation proceeds, keep each participating investigator informed of new observations discovered by or reported to the sponsor on the drug,

particularly with respect to adverse effects and safe use. Such information may be distributed to investigators by means of periodically revised investigator brochures, reprints or published studies, reports or letters to clinical investigators, or other appropriate means. Important safety information is required to be relayed to investigators in accordance with 21 C.F.R. § 312.32." 21 C.F.R. § 312.55.

26. Federal law has clearly established a longstanding policy providing for strong protections for human subjects in clinical trials.[10] With respect to patients in clinical trials, "no investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject." 21 C.F.R. § 50.20. "No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence." *Id*. In seeking informed consent, among other things, the following information shall be provided to each subject: (i) "a description of any reasonably foreseeable risks or discomforts to the subject," and (ii) "for research involving more than minimal risk . . . an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained." 21 C.F.R. § 50.25. Here, Juno provided its investigators with an investigator's brochure and a sample/model form/proposed informed consent document for use in the ROCKET Trial that was required to describe the risks and side effects associated with JCAR015. The FDA had not approved any warnings for such risks and side effects for JCAR015.

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[10] *See, e.g.,* 44 F.R. 47713 (Aug. 14, 1979); 46 F.R. 8942 (Jan. 27, 1981); 56 F.R. 28003 (June 18, 1991); 56 F.R. 28025 (June 18, 1991); 60 F.R. 183 (Sept. 21, 1995); 60 F.R. 246 (Dec. 22, 1995); 61 F.R. 215 (Nov. 5, 1996); 64 F.R. 54180 (Oct. 5, 1999).

III. Juno's CD19 Product Candidates have a well-documented history of severe and devastating side effects, including causing multiple deaths.

27. Buried in its single-spaced, 304 page 2015 Annual Report, Juno admits that the "use of our product candidates could be associated with side effects or adverse events which can vary in severity from minor reactions to *death* and in frequency from infrequent to prevalent. . . . We have seen severe neurotoxicity or [severe cytokine release syndrome], in some cases leading to *death*, in a number of patients . . . using each of JCAR015, JCAR017, and JCAR014."[11]

28. Juno further admitted in its Juno Securities Lawsuit Answer that "Car-T therapy can have serious and deadly side effects, including *severe neurotoxicity* that can damage the brain and cause *cerebral edemas and death*."[12]

29. In addition to burying relevant material information regarding the risks of its CD19 Product Candidates in SEC filings, Juno's knowledge of such risks is also evidenced by various papers and presentations that it, its officers, employees, agents, and researchers working on its clinical trials, published in various publications or presented to various conferences and meetings, including, without limitation, the American Society of Hematology, the American Society of Clinical Oncology Conference, the International Conference on Immunotherapy in Pediatric Oncology, the American Association for Cancer Research, Jefferies Global Healthcare Conference, Goldman Sachs Global Healthcare Conference, Morgan Stanley Global Healthcare Conference, and the Leerink Partners Rare Disease & Immune-Oncology Roundtable Conference.

30. As discussed below, Juno omitted and failed to disclose this material information to Maty prior to obtaining her purported informed consent to participate in the JCAR015 Phase II

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[11] *Id*. at 72 (emphasis added).

[12] Juno's Securities Lawsuit Answer, ¶ 28 (emphasis added).

ROCKET Trial. Juno thereby misrepresented the risks of the ROCKET Trial to Maty and robbed her of a sufficient and reasonable opportunity to make a truly informed decision whether she should participate in the ROCKET Trial rather than participating in another clinical trial being conducted by one of Juno's competitors, or deciding to continue traditional treatments for her ALL. In sum, Juno failed to provide Maty a fair and adequate warning of the serious and deadly side effects of JCAR015.

A. JCAR015

31. As of February 29, 2016, when Juno issued its 2015 Annual Report, JCAR015 was Juno's "most advanced development product candidate."[13] In January 2007, an IND application for JCAR015 was submitted to the FDA by Memorial Sloan Kettering Cancer Center in New York City ("MSK").[14] In January 2010, MSK, as sponsor and investigator, initiated a Phase I clinical trial for JCAR015 to treat ALL entitled "Precursor B Cell Acute Lymphoblastic Leukemia (B-ALL) Treated with Autologous T Cells Genetically Targeted to the B Cell Specific Antigen CD19."[15] This Phase I trial for JCAR015 was not expected to be completed until January 2017.[16]

32. But even the early results from the Phase I trial, which Juno reported to certain sectors of the medical community, in its Annual Reports to the SEC, and various investment banks, while concealing such information from its clinical trial participants, establish that JCAR015 had serious safety risks and call into question Juno's "fast to market strategy" of proceeding with the Phase II ROCKET Trial at all – a decision that would have deadly

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[13] 2015 Annual Report, at 16.

[14] *Id*.

[15] *Id*.; https://clinicaltrials.gov/ct2/show/NCT01044069.

[16] https://clinicaltrials.gov/ct2/show/NCT01044069; Juno Securities Lawsuit Answer, ¶ 35.

consequences for Maty and other patients.

33. According to the 2015 Annual Report, "[t]he *notable side effects* of JCAR015 are *severe cytokine release syndrome ("sCRS")* and *severe neurotoxicity*.[17] As discussed below, this single sentence, buried in a single-spaced, 304 page SEC filing, discloses more material and truthful information regarding JCAR015's risks than the purported informed consent document given to Maty to sign.

34. Juno's 2015 Annual Report further explains that "sCRS is a condition that, by convention, is currently defined clinically by certain side effects, including hypotension, or low blood pressure, when such side effects are serious enough to lead to intensive care unit care with mechanical ventilation or significant vasopressor support. CRS is generally believed to result from the release of inflammatory proteins in the body as the CAR T cells rapidly multiply in the presence of the target tumor proteins."[18]

35. According to the 2015 Annual Report, "[s]evere neurotoxicity can have several clinical manifestations, including confusion, aphasia, encephalopathy, myoclonus and generalized seizure. Severe neurotoxicity is defined as events having grade 3 or higher severity as defined by Common Terminology Criteria for Adverse Events ("CTCAE") for each manifestation. These severe neurotoxicity events may require ICU level care."[19]

36. Given the severity of these two "notable side effects" of JCAR015, which both require, by Juno's own definition, "ICU level care," it is unfortunately not shocking that, according to the 2015 Annual Report, "[i]n early 2014, *two patient deaths* in the JCAR015 trial,

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[17] 2015 Annual Report, at 18 (emphasis added).

[18] *Id*.

[19] *Id*.

which we believe were either directly or indirectly related to sCRS, resulted in the FDA placing the trial on clinical hold."[20] Juno further reported in the 2015 Annual Report that "[s]everal JCAR015 protocol changes were made after those deaths . . . resulted in the FDA removing the clinical hold," but Juno also warned that "these protocol changes . . . may not result in a better tolerability profile" and that "[s]ide effects such as toxicity or other safety issues associated with the use of our product candidates could also require us . . . to perform additional studies or halt development or sale of these product candidates."[21] As discussed below, Juno's warning would tragically prove to be correct.

37. As of November 2, 2015, the data Juno presents in its 2015 Annual Report regarding the prevalence of these devastating side effects – severe cytokine release syndrome and severe neurotoxicity – is truly staggering:[22]

Summary of Clinical Data
JCAR015

	Disease Burden(1)		
	Minimal Residual	Morphologic(2)	Total
Number of Patients	21	25(3)	46(3)
Complete Remission(4)	19/21 (90%)	18/24 (75%)	37/45 (82%)
Complete Molecular Remission(5)	15/21 (71%)	15/24 (63%)	30/45 (67%)
Severe CRS(6)	0/21 (0%)	11/25 (44%)	11/46 (24%)
Grade 3 and Above Neurotoxicity	3/21 (14%)	10/25 (40%)	13/46 (28%)

(1) Minimal residual disease = presence of no more than 5% lymphoblasts in a patient's bone barrow; morphologic disease = more than 5% lymphoblasts in a patient's bone marrow
(2) Includes one subject with extra-medullary disease only
(3) Includes one subject who was evaluable for safety outcomes, but not for efficacy
(4) Includes both complete remission and complete remission with incomplete hematological recovery
(5) Measured by flow cytometry or PCR
(6) Defined as requiring mechanical ventilator or significant vasopressor support

38. This chart from Juno's 2015 Annual Report summarizes JCAR015 clinical data for ALL patients and does not account for patients with other types of cancers.[23] Of the 46 ALL patients, 24 of them (or 52 percent) suffered from either severe cytokine release syndrome or severe neurotoxicity, with 24 percent suffering severe cytokine release syndrome and 28 percent

[20] *Id*. at 72 (emphasis added).
[21] *Id*.
[22] *Id*. at 17.
[23] *Id*. at 17 & 19.

suffering from severe neurotoxicity.[24]

39. And the data is much worse when one focuses on the morphologic patient population of the study, which Juno defines as those patients with more than 5% lymphoblasts in their bone marrow: 21 of the 25 ALL patients (84 percent) suffered from severe cytokine release syndrome or severe neurotoxicity, with 44 percent suffering severe cytokine release syndrome and 40 percent suffering from severe neurotoxicity.

40. To put these numbers in perspective, the ROCKET Trial's informed consent document categorized side effects occurring in more than 20 percent of patients as "common," which is the category delineating the most frequently occurring side effects.[25] Thus, Juno should have listed severe cytokine release syndrome and severe neurotoxicity as "common" side effects of JCAR015 but did not do so. And, as discussed below, none of this information was disclosed in the ROCKET Trial informed consent document signed by Maty, as "common" or "occasional" or "rare" or otherwise.

41. Incredibly, despite these remarkable numbers and the two Phase I patient deaths, Juno claims in its 2015 Annual Report that "[o]ther than [severe cytokine release syndrome] and severe neurotoxicity, JCAR015 has been generally well tolerated."[26]

42. Equally incredible is that, despite these remarkable side effect/toxicity statistics and the two Phase I patient deaths, Juno, operating under its "fast to market strategy;" recklessly advanced JCAR015 to a Phase II trial, dubbed the ROCKET Trial, on August 21, 2015 –

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[24] *Id*.

[25] Informed Consent/Authorization for Participation in Research with Option Procedures for The ROCKET Study: A Phase 2, Single-Arm, Multicenter Trial to Determine the Efficacy and Safety of JCAR015 in Adult Subjects with Relapsed or Refractory B-Cell Acute Lymphoblastic Leukemia, 2015-0140, Date of Consent Activation, May 2, 2016 ("ROCKET Trial Informed Consent"), at 13, attached as Exhibit 1.

[26] 2015 Annual Report, at 19.

approximately 17 months before the Phase I trial was originally supposed to end in January 2017.[27] Given that the Phase II ROCKET Trial wasn't scheduled to be completed until January 2017,[28] Juno's representations that the ROCKET Trial "could support accelerated U.S. regulatory approval as early as 2017"[29] are not only highly suspect, as a Phase III trial and the NDA and approval process could not have occurred in the two remaining months of 2017, but they also served as a harbinger of what was to come from Juno's reckless "fast to market strategy" – five more patients would lose their lives before Juno finally terminated its ill-fated JCAR015 clinical trials.

B. JCAR014

43. Although Juno does not plan to move JCAR014 into registration trials, it is sufficiently similar to the other CD19 Product Candidates that Juno has reported that it is using the JCAR014 trial data to provide "insights on how to improve our efficacy and safety in patients . . . across our portfolio."[30] JCAR014 also targets CD19 and has been evaluated in a Phase I/II trial for adults with ALL, as well as other types of cancer, at the Fred Hutchinson Cancer Research Center in Seattle.[31]

44. As with JCAR015, Juno administered a round of pre-conditioning chemotherapy to patients, with some patients receiving cy and some patients receiving a combination of flu and cy.[32]

45. Also as with JCAR015, JCAR014 has "displayed a side effect profile that is

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[27] *Id*. at 22; https://clinicaltrials.gov/ct2/show/NCT01044069; Juno's Securities Lawsuit Answer, ¶ 35; https://clinicaltrials.gov/ct2/show/NCT02535364?term=NCT02535364&rank=1

[28] https://clinicaltrials.gov/ct2/show/NCT02535364?term=NCT02535364&rank=1

[29] 2015 Annual Report, at 4-5; Juno Securities Lawsuit Answer, ¶ 35.

[30] 2015 Annual Report, at 3-4.

[31] *Id*. at 24.

[32] *Id*. at 24-25.

similar to our other CD19-directed product candidates in the types of adverse events observed," including a high degree of severe cytokine release syndrome and severe neurotoxicity.[33] In this trial, nearly three quarters of the ALL patients suffered from one of these devastating side effects, with 23 percent experiencing severe cytokine release syndrome and 50 percent experiencing severe neurotoxicity.[34]

46. In the JCAR014 trial, there have been three ALL patient deaths, two NHL patient deaths, and one CLL patient death, all attributable to severe cytokine release syndrome and/or severe neurotoxicity.[35]

47. Juno's 2015 Annual Report disclosed JCAR014 data that it deemed to "provide[] important insights" indicating that the patients receiving the combination of flu and cy were at a significantly greater risk than patients who only received cy:[36]

JCAR014: NHL Experience Provides Important Insights

Conditioning Regimen	Non-Flu/Cy	Flu/Cy		
Dose Level	All Doses N=12	2*10⁵/kg N=3	2*10⁶/kg N=11	2*10⁷/kg N=4–6
Efficacy				
CR	1/12 (8%)	1/3 (33%)	7/11 (64%)	1/4 (25%)
CR/PR	6/12 (50%)	1/3 (33%)	9/11 (82%)	3/4 (75%)
Toxicity				
sCRS	0/12 (0%)	0/3 (0%)	1/11 (9%)	3/6 (50%)
Severe Neurotoxicity	2/12 (17%)	1/3 (33%)	2/11 (18%)	4/6 (67%)

48. This data indicates that 11 of the 20 flu/cy patients at all doses (55 percent) suffered from severe cytokine release syndrome or severe neurotoxicity, with 20 percent suffering from severe cytokine release syndrome and 35 percent suffering from severe neurotoxicity. Meanwhile, none of the 12 non-flu/cy patients suffered from severe cytokine

[33] *Id*.
[34] *Id*. at 24.
[35] *Id*. at 24-26; 2016 Annual Report, at 17-19.
[36] 2015 Annual Report, at 25.

release syndrome, and only 2 of the 12 non-flu/cy patients (17 percent) suffered from severe neurotoxicity. These are indeed "important insights."

IV. Maty Holland and her tragic participation in Juno's ROCKET Trial.

49. Maty was born on February 10, 1997 and was first diagnosed with ALL at the age of 13, on February 24, 2010. Maty responded well to a multi-year course of conventional chemotherapy and went into remission at the start of her freshman year at Champion High School in Boerne, Texas, where she finished fourth in her class of 333 students. She was a member of the freshman homecoming court, a JV cheerleader, the school varsity mascot "Charlie," and a member of the National Honor Society. She was active in her church. She was a model for 4 years in the American Cancer Society's Ranch Chic Fashion Show. Maty eventually chose to attend Baylor University over other schools, such as Texas A&M University and the University of Southern California, where she was also accepted to continue her education. At Baylor, Maty was first runner-up in the Miss Green and Gold Pageant and played intramural girls flag football for "Earle's Pearls." Maty was a very intelligent, vivacious and beautiful young woman, who aspired to be a doctor, so she could help other young adults suffering from ALL.

50. During a routine checkup with her oncologist in San Antonio, Dr. Mahendra Patel, during the winter break of her freshman year at Baylor, it was discovered that Maty's platelets were low. More bloodwork and a bone marrow aspiration revealed that her ALL had relapsed, as her lymphoblast cells were at 85 percent. After her first chemotherapy treatment, they went down to 28 percent, but after four more rounds of chemotherapy, her lymphoblasts did not reach 0.1 percent.

51. While Maty could have explored other treatment options, Dr. Patel informed her of CAR-T immunotherapy, which he described as "the cutting edge," and suggested she see a

pediatric oncologist at M.D. Anderson, Dr. Michael E. Rytting.

52. Maty and her parents met with Dr. Rytting on May 5, 2016. Dr. Rytting informed them that there was an adult CAR-T trial for ALL that Maty could potentially be a candidate for, which would later be identified as Juno's Phase II JCAR015 ROCKET Trial.

A. Juno's paid investigator, Dr. Wierda, touts the potentially positive aspects of the ROCKET Trial to Maty while failing to discuss the deadly side effects.

53. Dr. William Wierda was M.D. Anderson's Study Chair, or investigator, for the ROCKET Trial. Dr. Wierda was not a prescribing physician, but an investigator for the ROCKET Trial, charged with following the study protocol established by Juno for administering JCAR015 to Maty after her enrollment. There were no alternate available drugs for Dr. Wierda to choose from for the ROCKET Trial, but only one—JCAR015. Additionally, Dr. Wierda was disclosed in the informed consent document that Maty signed as having a "significant financial relationship" with Juno as a paid consultant and was thereby incentivized to enroll participants in and complete the ROCKET Trial at M.D. Anderson. In addition to receiving compensation and research funding from Juno, Dr. Wierda also received compensation as a consultant and/or research funding from AbbVie, Karyopharm, Genentech/Roche, Merck, Pharmacyclics, Gilead, Sanofi, Genzyme, Kite, GSK/Novartis, Emergen, Celgene, and Janssen, two of which – Kite and Novartis – are direct CAR-T competitors of Juno that have received FDA approval for their CAR-T immunotherapies.[37]

54. The leukemia team at M.D. Anderson was presented with Maty's case on May 10, 2016 and decided that Maty met the eligibility criteria and could be enrolled in the ROCKET

[37] Shah BD, Stock W, Wierda WG, et al. Phase 1 Results of ZUMA-3: KTE-C19, an Anti-CD19 Chimeric Antigen Receptor (CAR) T Cell Therapy, in Adult Patients with Relapsed/Refractory Acute Lymphoblastic Leukemia (R/R ALL), Presented at: 59th Annual ASH Meeting, Atlanta, GA, December 11, 2017. Oral Presentation 888.

Trial, pending additional pre-screening testing and Maty's agreement to participate. Dr. Wierda was a member of the leukemia team that determined that Maty was an eligible candidate for the ROCKET Trial.

55. Maty and her mother returned to Houston on May 16, 2016, when, at their specific request, they met Dr. Wierda for the first time. During this meeting, Dr. Wierda generally discussed the ROCKET Trial with Maty and her mother, including that Maty was an eligible candidate for the trial, and he informed them of the positive remission rates being obtained in CAR-T immunotherapy trials. Notably, Dr. Wierda did not discuss of any risks or side effects to participants in the ROCKET Trial during this meeting. Thus, while being paid by Juno to conduct the ROCKET Trial, Dr. Wierda touted the positive aspects of the ROCKET Trial – possible remission – and ignored the negative aspects of the ROCKET Trial – the potentially deadly side effects. Dr. Wierda also discussed the pre-screening process for the trial and the schedule for the various steps in the process. He also answered Maty and her mother's questions.

56. Immediately after meeting with Dr. Wierda, Maty and her mother were escorted to another room where they met with Virginia Bayer, M.D. Anderson's Lead Clinical Research Nurse for the ROCKET Trial, who reported to Dr. Wierda. As Lead Clinical Research Nurse for the ROCKET Trial, Bayer's responsibilities included guiding participants through the informed consent process, collecting data for the trial, managing the clinical and operational aspects of the clinical trial protocol, ensuring that participants meet protocol goals, and providing information to both the participants and the principal investigator, Dr. Wierda.

57. During this meeting, Bayer provided further information regarding the ROCKET Trial and answered Maty and her mother's questions. Bayer walked Maty and her mother through the ROCKET Trial Informed Consent Form during this meeting, and Maty signed the

form. Contrary to the representation in that document, Maty was not given a copy of the signed document. After, and as a result of these meetings with Dr. Wierda and Bayer, Maty agreed to participate in the ROCKET Trial. During this meeting, nothing was said to Maty and her mother about the significant known risks to patients in the ROCKET Trial of suffering from severe neurotoxicity, severe cytokine release syndrome, or cerebral edema, leading to death, after their infusion with JCAR015.

58. Dr. Wierda was not present during the discussion of the ROCKET Trial Informed Consent Form and was not available to answer questions regarding the Informed Consent. Thus, Dr. Wierda was not a conduit for any warnings of the deadly risks of JCAR015 from Juno to Maty.

59. Maty spent the next four days completing prescreening testing and having her white blood cells harvested for delivery to Juno's lab in Seattle to be genetically modified.

B. The ROCKET Trial Informed Consent

60. On May 16, 2016, Maty signed the ROCKET Trial Informed Consent.[38] A stated purpose of the Informed Consent was to describe the possible risks connected with being in the ROCKET Trial. As discussed above, as the sponsor of the ROCKET Trial, Juno was required, under federal regulations, to inform the clinical trial participants of the reasonably known risks of the ROCKET Trial through Juno's investigators, including Dr. Wierda, to whom Juno was required to provide full and fair disclosure, an adequate warning, and not misleading information regarding adverse effects and safety issues related to JCAR015. The information regarding the risks and side effects of JCAR015 was provided Dr. Wierda and M.D. Anderson by Juno through

[38] ROCKET Trial Informed Consent, attached as Exhibit 1. As is the norm for informed consents in clinical trials, Juno's Informed Consent was not approved by the FDA. Rather, under federal law, it is the investigators' and/or sponsors' institutional review boards ("IRBs") that are responsible for, among other things, approving the informed consent document.

an Investigator's Brochure for inclusion in the Informed Consent. For the ROCKET Trial, Juno provided its investigators four different versions of its Investigator's Brochure, the most recent of which is dated October 27, 2015. Neither Maty nor her mother ever saw the Investigator's Brochure.

61. Given the prevalence of the known deadly side effects of JCAR015 set forth above, Juno breached its duty to provide full and fair disclosure to Dr. Wierda and M.D. Anderson and, thereby, its clinical trial participants, because the Informed Consent was woefully inadequate and wholly failed to disclose reasonably foreseeable risks of the ROCKET Trial. The Informed Consent states that "[t]he more commonly occurring side effects are listed in this form, as are rare but serious side effects."[39] But the Informed Consent omits and fails to disclose the well-known and deadly side effects of JCAR015 – severe cytokine release syndrome[40] or severe neurotoxicity, both of which, by Juno's own definitions, require ICU-level care, and, as discussed above, were sufficiently prevalent that Juno's own data suggests they should have been listed as "common" side effects. The Informed Consent further omits and fails to disclose the risk of cerebral edema. While it mentions cytokine release syndrome, it minimizes and understates the severity of that condition, and does not warn the trial participants of the increased level of risk for developing severe cytokine release syndrome. Warning its investigators and trial participants of a much lower risk than the actual risk renders such a warning not only misleading, but

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[39] *Id*. at 9.

[40] Although the Informed Consent does mention "cytokine release syndrome," *Id*. at 10, by Juno's own definitions, "cytokine release syndrome" is clearly not the same as "severe cytokine release syndrome." Cytokine release syndrome describes the symptoms associated with the release of cytokines – inflammatory proteins – in the body, which is not unique to immunotherapy treatment or cancer in general. 2015 Annual Report, at 18. Indeed, cytokines are released in the body due to causes as mundane and unremarkable as a hangover. *See* Dai-Jin Kim, Won Kim, Su-Jung Yoon, Bo-Moon Choi, Jung-Soo Kim, Hyo Jin Go, Yong-Ku Kim, Jaeseung Jeong, Effects of alcohol hangover on cytokine production in healthy subjects, In Alcohol, Volume 31, Issue 3, 2003, Pages 167-170, ISSN 0741-8329, https://doi.org/10.1016/j.alcohol.2003.09.003. In contrast, Juno acknowledges that severe cytokine release syndrome requires, at minimum, ICU-level care and can lead to death. 2015 Annual Report, at 18.

ineffective.

62. In addition, Juno falsely claims in the Informed Consent that "[t]his is an early study of JCAR015, so the side effects are not well known."[41] The Informed Consent omits and fails to disclose that multiple patients, who participated in clinical trials for JCAR-015, had died after their infusion with JCAR-015. But it is clear from Juno's annual reports, its own medical literature and presentations, and medical literature and presentations authored by third parties, that the side effects of JCAR015 were certainly well known to Juno. Juno's 2015 Annual Report, issued approximately three months before Maty signed the Informed Consent, expressly stated that "[t]he *notable side effects* of JCAR015 are *severe cytokine release syndrome ("sCRS")* and *severe neurotoxicity*.[42] Furthermore, the Informed Consent was prepared/revised after the release of Juno's 2015 Annual Report.

63. And putting aside the fact that JCAR015 should have never progressed into a Phase II trial, this was not "an early trial." Rather, by this point in time, the JCAR015 Phase I trial had been operating for more than six years, and Juno had ample data to ascertain the side effects of the JCAR015 clinical trial so that it could truthfully communicate the reasonably known risks to the clinical trial participants in the Informed Consent.

64. Yet another defect with the Informed Consent is that it fails to disclose the significantly elevated risks of suffering from severe cytokine release syndrome and severe neurotoxicity if the patient is considered "morphologic," or having more than 5 percent lymphoblasts in their bone marrow, which are clearly set forth in Juno's 2015 Annual Report.

65. Again, the 2015 Annual Report discusses "important insights" showing a significantly higher incidence of severe cytokine release syndrome and severe neurotoxicity in

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[41] ROCKET Trial Informed Consent, attached as Exhibit 1, at 10.
[42] 2015 Annual Report, at 18 (emphasis added).

patients receiving the flu/cy combination. But the Informed Consent makes no mention of this "important insight," and merely lists the side effects of flu taken in isolation and cy taken in isolation – with no mention of the side effects of the flu/cy combination.

66. Because the ROCKET Trial clearly contained "more than minimal risk," the Informed Consent was also required to contain "an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained." 21 C.F.R. § 50.25. Juno's Informed Consent contained none of this information.

67. Had Juno disclosed the truth to Maty, and what federal law requires for legally effective informed consent, Maty would not have signed the Informed Consent and agreed to participate in the ROCKET Trial. Rather, she and her parents would have explored other treatment options and/or other competing clinical trials. Maty was not in a condition that the ROCKET Trial was her only choice.

C. The first ROCKET Trial patient dies. In response, Juno issues a misleading press release praising JCAR015, and its CEO and CFO subsequently sell millions of dollars worth of Juno stock.

68. Following the multiple deaths stemming from the Phase I trial, it did not take long for history to repeat itself with the ROCKET Trial. On May 24, 2016, Max Vokhgelt, a participant in the ROCKET Trial, died from severe cytokine release syndrome and severe neurotoxicity at Washington University School of Medicine in St. Louis.[43]

69. But rather than disclose this death to the public, the FDA, and its clinical trial participants, just eleven days later, on June 4, 2016, Juno chose to issue a press release that extolled the virtues of JCAR015, entitled "Juno Therapeutics' Investigational CAR T Cell

[43] https://www.statnews.com/2016/12/12/juno-patient-death-cancer-immunotherapy/

Product Candidate JCAR015 Shows High Response Rates in Adults with B-cell ALL."[44] In this press release, Juno, referring to the data from its Phase I trial, "announced that encouraging clinical data from JCAR015 . . . support its strategic approach towards the commercialization of its first CAR T therapy," and Juno's Chief Medical Officer, Mark J. Gilbert, M.D., stated that "[t]hese findings provide us with further confidence about our development strategy and the ongoing Phase II ROCKET pivotal trial."[45] But the press release contains no mention of any of the Phase I trial deaths or the death that had occurred just days earlier in the ROCKET Trial. Not surprisingly, this press release caused Juno's stock price to soar 16.5% in a single day – from $42.65 to $49.72.

70. Certain Juno insiders profited handsomely from this glowing, yet misleading, press release. Juno's CEO Hans Bishop sold over $8.6 million worth of Juno stock between June 6, 2017 – two days after the press release – and June 30, 2017. Juno's CFO and Head of Corporate Development, Steven Harr, sold about $1.3 million worth of Juno stock, following the press release, on June 10, 2016. Hans Bishop will reportedly receive a payout up to $287 million from Celgene Corporation's buyout of Juno for his shares, stock options and stock units.

D. After the first ROCKET Trial death, Maty and her family are further misled about the risks involved.

71. Meanwhile, in early June 2016, Bayer called Plaintiff Butler regarding a "new safety concern" and advised that Dr. Wierda would later explain the details. Bayer further advised that the trial was "on hold" for new participants until a "new informed consent form" was released, but that since Maty and another patient had already been approved, had their white

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[44] http://ir.junotherapeutics.com/news-releases/news-release-details/juno-therapeutics-investigational-car-t-cell-product-candidate

[45] *Id*.

blood cells harvested and in Juno's lab in Seattle, they could continue in the trial once the new informed consent form was ready.

72. On June 15, 2016, Maty and her mother met with Dr. Wierda, who explained that the "new safety concern" was that a patient had recently died after developing a high fever in the first 24 hours of the T cell infusion, unlike all other previous participants. Upon receiving this news, Maty and her mother expressed reluctance regarding the trial and questioned whether it was safe. In response, Dr. Wierda downplayed the risks of the ROCKET Trial, claiming that by aggressively administering steroids, within the first 24 hours of the infusion, the cerebral edema the patient developed after the infusion might have been reversed. Dr. Wierda further stated that because of the high fever, no steroids were given this patient to avoid T cell suppression. Plaintiff Butler asked Dr. Wierda if there was a new informed consent form and was told it was not yet ready. Dr. Wierda advised that he thought Maty would do fine, and that if a high fever occurred, they would simply administer steroids right away.

73. Thus, if Dr. Wierda, Juno's paid agent/investigator, knew of the true risks of JCAR015 and the ROCKET Trial, he failed to disclose and misrepresented what were known deadly side effects of JCAR015. If Dr. Wierda did not know of the true risks of JCAR015 and the ROCKET Trial, then Juno did not adequately warn its own investigators regarding the known deadly side effects of JCAR015. In either event, Juno failed to disclose the known risks and side effects of JCAR015 and the ROCKET Trial to Maty.

74. In addition, Juno failed to update its investigator's brochure following the May death, and prior to Maty's infusion with JCAR015, so no updated informed consent form was ever provided to Maty, as was previously represented. It is unclear where Dr. Wierda obtained the information provided to Maty and her mother, discussed above, that significantly understated

the risks of the ROCKET Trial by creating the false impression that the deadly effects of JCAR015 were reversible, but, as discussed below, this information was completely wrong. Thus, not only did Dr. Wierda play a significant role in Maty initially agreeing to participate in the ROCKET Trial, but he also played a critical role in preventing Maty from declining to continue in the trial following the May death. Maty's T cells were already harvested and she was prepared for her infusion with her modified T cells. To lose her as a participant in the Rocket Trial would not further Juno's "fast to market" strategy.

75. That same day, Maty proceeded with the ROCKET Trial, completing the remaining lab work, chest x-ray, spinal tap, bone marrow aspiration, and skin biopsy over the next two days. Maty's lymphoblasts were at 70 percent, putting her in the higher-risk morphologic category for severe cytokine release syndrome and severe neurotoxicity, although unbeknownst to her and her parents.

E. Maty proceeds with the ROCKET Trial and becomes another victim of Juno's fatal "fast to market" strategy.

76. Maty was admitted to M.D. Anderson on June 16, 2016. Starting on the following day, she began her pre-conditioning chemotherapy. Maty was chosen to receive the flu/cy combination, putting her in the higher-risk category for severe cytokine release syndrome and severe neurotoxicity. Maty received cy on June 17 and flu on June 18-20, with three doses over the three day period.

77. Juno's genetically modified CAR-T cells were infused into Maty on June 23, 2016. Four days later, on June 27, she began suffering from high fevers, in excess of 103.5 degrees. Severe neurotoxicity started setting in the next day, June 28, as Maty began deteriorating and becoming increasingly nonresponsive.

78. Dr. Wierda arrived at Maty's room on June 29 and advised Plaintiff Butler that

neurotoxicity was "common" and "reversible." That same afternoon, Maty began experiencing severe seizures that became virtually nonstop, and she was transferred to the ICU, where she somewhat stabilized.

79. The following morning, June 30, 2016, the ICU nurses informed Plaintiff Butler of a "crisis situation" with Maty, which involved "cerebral bleeding or edema," and one of her pupils failing to dilate. A CAT Scan taken shortly thereafter revealed irreversible cerebral edema. Maty continued to deteriorate. Dr. Wierda returned to the ICU shortly before Maty's ventilator was turned off, and he informed Plaintiff Butler for the first time that "we believe the cerebral edema was due to the addition of flu" to the pre-conditioning chemotherapy.

80. Maty Holland died on June 30, 2016, at the age of 19. The causes of death listed on her death certificate are: (i) severe cerebral edema, (ii) status epilepticus, and (iii) cytokine release syndrome.

81. On the same day that Maty died, Juno's CEO, Hans Bishop, sold over $4 million worth of Juno's stock, in addition to the millions more in Juno stock he previously sold following the May death in St. Louis, discussed above.

82. Another patient in the ROCKET Trial would go on to die the same week that Maty died. It was not until July 7, 2016 that Juno would finally publicly announce the three deaths from May and June 2016, after initially misstating the number of deaths that had occurred and having to correct the misstatements in amended SEC filings. After a very brief FDA clinical hold, in which flu was removed from the protocol and Juno was instructed to prepare a new informed consent form, Juno was given permission to resume the ROCKET Trial.

83. Just four months later, in November 2016, two more patients died in the ROCKET Trial. Juno voluntarily put the ROCKET Trial on hold again while it conducted an

investigation. Subsequently, in March 2017, Juno finally made the decision to permanently terminate further development of JCAR015 – but only after at least seven patients died in the combined Phase I and Phase II JCAR015 trials, not to mention the, at minimum, six other patients who died in the JCAR014 trials.

84. Clearly, Juno's "fast to market" strategy for JCAR015 was a human disaster. But even the decision to advance JCAR015 to a Phase II trial was highly suspect, if not reckless, given the high prevalence of severe toxicities that Juno reported from the Phase I trial: nearly 57 percent of the participants suffered from severe cytokine release syndrome (14/51 or 27 percent) or severe neurotoxicity (15/51 or 29 percent).[46] And the results from the Phase II ROCKET Trial were even worse: nearly 74 percent of the participants suffered from severe cytokine release syndrome (8/38 or 21 percent) or severe neurotoxicity (20/38 or 52 percent).[47] Although neurotoxicity and cytokine release syndrome are side effects of CAR-T immunotherapies in general, the severity and rate of JCAR015's side effects were much higher than those present in other studies, including Juno's competitors that have since received FDA approval for their product candidates.

85. After the two November 2016 deaths, and its investigation regarding the cause of JCAR015's high rate of severe side effects and resulting deaths, Juno announced one year later that JCAR015's fatal severe cytokine release syndrome and severe neurotoxicity were attributed to early and rapid modified CAR-T cell expansion and a rise in interleukin (IL)-15 levels.[48]

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[46] *See*, *supra*, n. 43.

[47] DeAngelo DJ, Ghobadi A, Park JH, et al. Clinical Outcomes for the Phase 2, Single-Arm, Multicenter Trial of JCAR015 in Adult B-ALL (ROCKET Study). Presented at: 32nd Annual SITC Meeting, National Harbor, MD, November 8-12, 2017. Poster P217.

[48] Gilbert MJ. Severe Neurotoxicity in the Phase 2 Trial of JCAR015 in Adult B-ALL (ROCKET Study): Analysis of Patient, Protocol and Product Attributes. Presented at: 32nd Annual SITC Meeting, National Harbor, MD, November 8-12.

86. In addition, Juno also claimed that certain patient-specific factors contributed to the severe side effects and deaths,[49] including, among other things, that "patients whose tumors expressed a non-Philadelphia type gene signature experienced greater toxicity. Among 15 patients with this type of genetic signature, 12 had Grade 3 or higher neurotoxicity, including all five patients who died," a result that Juno's Chief Medical Officer, Mark Gilbert, called "surprising."[50] Unfortunately, given Juno's dismal safety record with both JCAR014 and JCAR015, what is not surprising is that, either intentionally or negligently, Juno appears to have also seriously botched its investigation of JCAR015. The claim that all five patients who died expressed a non-Philadelphia type gene signature is false for two reasons. First, Maty was in fact positive for the Philadelphia gene, which is readily apparent from her prior medical records and those generated and used during the course of her participation in the ROCKET Trial. Second, Juno has demonstrated difficulties with accurately reporting how many people have died during its JCAR015 trials, as its own SEC filings indicate that at least seven – not five – deaths are attributable to JCAR015.

87. Maty was used by Juno as a human guinea pig in order to advance its reckless "fast to market" strategy and seek the lucrative profits that early FDA approval of JCAR015 would bring. Juno ignored the deadly risks this drug posed for participants in its clinical trials and failed to adequately warn them of such risks. Had Maty and her parents known of the true risks of her participation in the ROCKET Trial, Maty would have pursued other treatment options. Juno denied Maty a fair, reasonable and meaningful opportunity to make an informed decision whether to participate in the ROCKET Trial. In her circumstances, greed trumped

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[49] *Id*.

[50] https://www.biopharmadive.com/news/juno-analysis-of-shuttered-study-offers-clues-for-car-t/510634/

patient safety with disastrous results. Plaintiffs now bring this wrongful death and survival action to recover damages for the tortious conduct that Maty and they suffered at the hands of Juno.

CAUSES OF ACTION

88. Plaintiffs re-allege and incorporate by reference the facts and allegations set forth in the preceding paragraphs as if fully set forth herein.

I. Count 1: Wrongful Death

89. Pursuant to Section 71.002 of the Texas Civil Practice and Remedies Code, Juno is liable to Plaintiffs for Maty's wrongful death.

90. Among others, a decedent's surviving parents are the statutory beneficiaries for purposes of bringing a wrongful death action. *Id*. §71.004(a). Here, Plaintiffs are Maty's surviving parents and entitled to bring this action.

91. As set forth below, Juno is liable for damages arising from the injuries that caused Maty's death, because her injuries were caused by Juno's wrongful acts, omissions, neglect, carelessness, unskillfulness, or default, when acting alone, or by and through its officers, employees, investigators and agents, which include, without limitation, fraud, fraudulent concealment, breach of warranty, negligence and negligence per se, for failure to warn and obtain Maty's legally effective informed consent, products liability claims for marketing and design defects, and negligent misrepresentation. As set forth above, the prevalent and deadly side effects of JCAR015 known to Juno, severe neurotoxicity and severe cytokine release syndrome, caused Maty's death. In addition, Juno's negligent acts or omissions were a substantial factor in bringing about Maty's death, and but for them, Maty would not have died from severe neurotoxicity and severe cytokine release syndrome. Juno omitted and failed to disclose these risks to Maty in the Informed Consent prior to her entering the ROCKET Trial. Had Juno told the

truth and adequately disclosed the reasonably known risks of the ROCKET Trial, Maty would not have participated in the ROCKET Trial and would not have died from severe neurotoxicity and severe cytokine release syndrome. Maty, had she lived, would have been entitled to bring these actions for her injuries.

92. The damages Plaintiffs seek include compensatory damages, including, without limitation, pain and mental anguish, the loss of care, maintenance, support, services, society and companionship, advice, counsel, medical expenses, funeral and burial expenses, and reasonable contributions of a pecuniary value.

II. Count 2: Survival

93. Juno is further liable to the Estate of Maty Holland, Deceased under the Texas Survival Act, under which a decedent's heirs, or legal representatives, may bring, on behalf of the decedent's estate, actions for personal injuries the decedent sustained prior to her death. TEX. CIV. PRAC. & REM. CODE § 71.021.

94. The purpose of the Texas Survival Act is to continue the decedent's cause of action beyond death to redress the decedent's estate for the injuries the decedent suffered while alive. The actual damages sought are those described above. In addition, Juno is liable for exemplary damages as set forth below and pursuant to Section 71.009 of the Texas Civil Practice and Remedies Code because Maty's death was caused by Juno's wilful acts or omissions or gross negligence.

95. As set forth below, Juno is liable for damages arising from the injuries that caused Maty's death because her injuries were caused by Juno's wrongful acts, omissions, neglect, carelessness, unskillfulness, or default, when acting alone or by and through its officers, employees, investigators and agents, which include, without limitation, fraud, fraudulent concealment, breach of warranty, negligence and negligence per se, for failure to warn and

obtain Maty's legally effective informed consent, products liability claims for marketing and design defects, and negligent misrepresentation. As set forth above, the prevalent and deadly side effects of JCAR015 known to Juno, severe neurotoxicity and severe cytokine release syndrome, caused Maty's death. In addition, Juno's negligent acts or omissions were a substantial factor in bringing about Maty's death, and but for them, Maty would not have died from severe neurotoxicity and severe cytokine release syndrome. Juno omitted and failed to disclose these risks to Maty in the Informed Consent prior to her entering the ROCKET Trial. Had Juno told the truth and adequately disclosed the reasonably known risks of the ROCKET Trial, Maty would not have participated in the ROCKET Trial and would not have died from severe neurotoxicity and severe cytokine release syndrome.

III. Count 3: Strict Products Liability

96. Juno placed into the stream of commerce JCAR015, which is an unreasonably dangerous product by reason of multiple product defects, and is, therefore, strictly liable in tort to Plaintiffs for the injuries sustained by Maty and her death, because of JCAR015's defects.

97. As discussed in more detail below, JCAR015, as administered to Maty and other victims in the ROCKET Trial, suffered from both marketing and design defects. These defects existed at the time that JCAR015, the genetically modified T-cells, left Juno's hands. The marketing and design defects made JCAR015 unreasonably dangerous because the defects were deadly side effects and Juno failed to disclose and adequately warn Maty of the dangers of such deadly side effects. The defects were a producing cause of Maty's injuries, because she died from the very side effects of JCAR015 known to Juno, but which it failed to warn Maty. Had Maty and Plaintiffs known of the unreasonable dangers of JCAR015, Maty would not have participated in the ROCKET Trial and would not have died from the deadly side effects.

98. JCAR015 exhibited a marketing defect because Juno knew, or should have

known, of the potential risk of harmful and fatal side effects, including severe neurotoxicity and severe cytokine release syndrome, presented by JCAR015, yet Juno nevertheless marketed it through its clinical trials without adequately warning its investigators and clinical trial participants of the dangers involved. JCAR015 demonstrated a risk of harm for fatal severe neurotoxicity and severe cytokine release syndrome that was inherent in the product, or that arose from the intended use of the product. Juno knew or reasonably foresaw the risk of harm at the time JCAR015 was marketed to Maty in the ROCKET Trial. Under Texas law, in order for a warning to be adequate, it must provide a complete disclosure of the existence and extent of the risk involved and be of an intensity justified by the magnitude of the risk. Juno wholly failed to meet this standard. The absence of sufficient warnings or disclosures in the Informed Consent rendered JCAR015 unreasonably dangerous to Maty, and Juno's failure to warn constituted a causative nexus to Maty's death.

99. JCAR015 was also defectively designed when distributed because Juno's clinical trial participants exhibited an unjustifiable high rate of fatal side effects, including severe neurotoxicity and severe cytokine release syndrome. As discussed above, Juno has identified the design defects as early and rapid modified CAR-T cell expansion and a rise in interleukin (IL)-15 levels. JCAR015 was unreasonably dangerous (weighing the risk and utility) to the ROCKET Trial participants, including Maty. JCAR015 reached Maty and the other clinical trial participants without substantial change in the condition in which it was manufactured and distributed. The severity and rate of JCAR015's side effects were much higher than those present in other studies, including Juno's competitors, such as Kite and Novartis, who have produced safer CAR-T immunotherapies that have received FDA approval. The defective and unreasonably dangerous condition of JCAR015 was a producing cause of physical harm and death to Maty.

100. Thus, Juno is strictly liable for the actual damages suffered by Maty and Plaintiffs for JCAR015's marketing and design defects.

IV. Count 4: Fraud and Fraudulent Concealment

101. Under Texas law, in order for a warning to be adequate, it must provide a complete disclosure of the existence and extent of the risk involved and be of an intensity justified by the magnitude of the risk. As discussed above, Juno wholly failed to meet this standard by failing to disclose life-threatening and fatal side effects – severe cytokine release syndrome and severe neurotoxicity – and multiple patient deaths, all of which Juno had long known about and intentionally concealed from Maty.

102. Under the applicable FDA regulations, referenced above, Juno had a duty to disclose the reasonably known risks of JCAR015 to its investigators and Maty. Juno further had a duty to disclose, because it voluntarily disclosed partial information, but failed to disclose the whole truth and made representations, but failed to disclose new information that made the earlier representations misleading or untrue. Juno defrauded Maty, by concealing material information regarding the known dangers of its CAR-T therapies and JCAR015, including their long and established history of severe neurotoxicity and severe cytokine release syndrome, and by failing to disclose numerous patient deaths during its clinical trials. The Informed Consent omitted and withheld this material information from Maty and affirmatively misrepresented the dangers of the ROCKET Trial and JCAR015. Maty was ignorant of such facts and had no reasonable opportunity to discover the truth prior to signing the Informed Consent. Juno is liable to Plaintiffs for the physical harm to, and death of, Maty, which resulted from Juno's fraud and fraudulent concealment against Maty, who relied upon Juno's misrepresentations and omissions of material facts in deciding whether to participate in the Rocket Trial. Juno intended and

expected its statements and omissions of material facts would induce Maty to participate in the ROCKET Trial, or should have realized that its misrepresentations and omissions of material facts were likely to induce Maty to participate in the ROCKET Trial. Juno knew, or should have known, its statements in the Informed Consent were false. The fraudulent representations of Juno, and its fraudulent concealment of material information, caused Maty's injuries and death.

V. Count 5: Negligence

103. As the sponsor of the ROCKET Trial, Juno owed Maty the duties to, among other things, use reasonable care in disclosing and warning of the reasonably known risks and side effects of JCAR015, designing JCAR015, and conducting the ROCKET Trial. Juno breached these duties by failing to disclose to and warn Maty of the reasonably known risks and deadly side effects of JCAR015, and by establishing a study protocol for the ROCKET Trial that permitted the administration of a drug with fatal side effects, including severe neurotoxicity and severe cytokine release syndrome. Under Texas law, in order for a warning to be adequate, it must provide a complete disclosure of the existence and extent of the risk involved and be of an intensity justified by the magnitude of the risk. Juno wholly failed to meet this standard. Juno's acts and omissions caused physical harm and death to Maty and, thus, proximately caused damages to Maty and Plaintiffs.

104. Further, Juno's acts and omissions constitute negligence per se, because they violated, without excuse, numerous FDA regulations, including, without limitation, 21 C.F.R. §§ 50.20, 50.25, 312.50, 312.55, and 312.32. Plaintiffs belong to the class that the relevant federal regulations were intended to protect and Maty's injury is of a type that the relevant regulations were designed to prevent.

VI. Count 6: Negligent Marketing

105. Juno had a duty to act according to an applicable standard of care, including the common law standard of care, discussed above, to use reasonable care in disclosing the reasonably known risks and side effects of JCAR015, and including complying with numerous federal FDA regulations, including, without limitation, 21 C.F.R. §§ 50.20, 50.25, 312.50, 312.55, and 312.32. Juno breached this standard of care by failing to disclose the reasonably known risks and side effects of JCAR015 to its investigators/agents and to its clinical trial patients and by establishing a study protocol for administering drugs with fatal side effects, including severe neurotoxicity and severe cytokine release syndrome. Under Texas law, in order for a warning to be adequate, it must provide a complete disclosure of the existence and extent of the risk involved and be of an intensity justified by the magnitude of the risk. Juno wholly failed to meet this standard. Juno's breach caused physical harm and death to Maty. There was a causal connection between Juno's breach of care and Maty's physical injuries and death because had Juno told the truth to Maty, she would not have participated in the ROCKET Trial and would not have died from severe neurotoxicity and severe cytokine release syndrome.

VII. Count 7: Negligent Misrepresentation

106. Through the Informed Consent, which, as discussed above, contained information about the severity and prevalence of the side effects of JCAR015 provided by Juno, Juno negligently gave, through its investigator, false information to Maty for her guidance in deciding whether to participate in the ROCKET Trial and upon which she reasonably and justifiably relied. Juno is, thus, subject to liability for the physical harm caused Maty. Under Texas law, in order for a warning to be adequate, it must provide a complete disclosure of the existence and extent of the risk involved and be of an intensity justified by the magnitude of the risk. Juno

wholly failed to meet this standard. Such harm actually occurred and resulted to Maty. Where such harm results to another, or to such third persons as Juno should expect to be put in peril by the action taken, Juno's negligence consisted of its failure to exercise reasonable care in ascertaining the accuracy of its information, or in the manner in which the information was communicated by Juno to its investigators and the participants in the ROCKET Trial. Its negligent misrepresentations proximately caused Maty's injuries and death.

VII. Breach of Warranty

107. Through the Informed Consent, Juno made express affirmations of fact regarding the ROCKET Trial and JCAR015. Juno's affirmations of fact in the Informed Consent were a part of the basis of the bargain, as the Informed Consent was required by federal law. Maty relied upon Juno's affirmations of fact in choosing to participate in the ROCKET Trial. The ROCKET Trial and JCAR015 failed to comply with Juno's affirmations of fact contained in the Informed Consent, as Juno misrepresented, and failed to disclose, the deadly side effects of the ROCKET Trial and JCAR015. Maty was injured by the failure of the ROCKET Trial and JCAR015 to comply with the express warranties contained in the Informed Consent. Such failure was the proximate cause of Maty's injuries. Juno was notified of the Plaintiffs' claims prior to filing suit.

EXEMPLARY DAMAGES

108. Plaintiffs re-allege and incorporate by reference the facts and allegations set forth in the foregoing paragraphs as if fully set forth herein.

109. The wrongful acts and/or omissions of Juno described herein were committed intentionally, knowingly, maliciously, wantonly and willfully, and in conscious disregard of the well-established rights of Maty and Plaintiffs. As a result of Juno's malice and actual fraud, Juno caused significant harm to Maty and Plaintiffs. Thus, Plaintiffs are entitled to recover exemplary

and/or punitive damages under TEX. CIV. PRAC. & REM. CODE §§ 41.003(a) & 71.009. In addition, because Juno's conduct constitutes a violation of Section 32.46 of the Texas Penal Code, exemplary damages in this action are not subject to the statutory cap.

CONDITIONS PRECEDENT

110. All conditions precedent to Plaintiffs' claims for relief have been performed or have occurred.

JURY DEMAND

111. Plaintiffs demand a trial by jury on all issues so triable.

PRAYER FOR RELIEF

For these reasons, Plaintiffs request that the Court issue citation for Defendant, Juno Therapeutics, Inc. to appear and answer, and that Plaintiffs be awarded a judgment against Defendant for the following:

a. actual damages;

b. nominal damages;

c. exemplary damages;

d. prejudgment and post-judgment interest;

e. court costs; and

f. any and all other relief, in law and in equity, both special and general, to which Plaintiffs are justly entitled.

Dated: October 1, 2018.

Respectfully submitted,

THE LANIER LAW FIRM, P.C.

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(Subject to Granting Pro Hac Vice Motion to Be Filed)

ATTORNEYS FOR PLAINTIFFS

CERTIFICATE OF SERVICE

I hereby certify that on this the 1st day of October, 2018, this instrument was electronically served on all parties registered through the Court's ECF system, and also by email delivery.

/s/ Christopher L. Gadoury
Christopher L. Gadoury